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EXAMINER	
DEVI, SARVAMANGALA J N	
ART UNIT	PAPER NUMBER
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/921,157	COVACCI ET AL.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *38 and 44-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38 and 44-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 08/256,848.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

REQUEST FOR CONTINUED EXAMINATION

1) A request for continued examination under 37 C.F.R 1.114, including the fee set forth in 37 C.F.R 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 C.F.R 1.114, and the fee set forth in 37 C.F.R 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 C.F.R 1.114. Applicants' submission filed on 04/04/05 has been entered.

Applicants' Amendment

2) Acknowledgment is made of Applicants' amendment filed 04/04/05 in response to the final Office Action mailed 11/03/04.

Status of Claims

3) Claims 38 and 44-46 have been amended via the amendment filed 04/04/05.

Claims 38 and 44-46 are pending and are under examination.

Prior Citation of Title 35 Sections

4) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

5) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Rejection(s) Maintained

6) The provisional rejection of claims 38 and 44 made in paragraph 9 of the Office Action mailed 10/15/02 and maintained in paragraph 6 of the Office Action mailed 03/03/04 and paragraph 12 of the Office Action mailed 11/03/04 under the judicially created doctrine of obviousness-type double patenting over the cited claims of the co-pending application, 09/360,934, is still maintained for reasons set forth therein. It is noted that Applicants have agreed to submit a terminal disclaimer over SN 09/360,934 upon indication of allowability of the claims.

7) The rejection of claims 45 and 46 made in paragraph 12 of the Office Action mailed 03/03/04 and paragraph 13 of the Office Action mailed 11/03/04 under provisionally rejected under

the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 40, 54, 61-65, 72-75, 82-86, 93 and 94 of the co-pending application, SN 09/360,934, is maintained for reasons set forth therein.

Rejection(s) Withdrawn

8) The rejection of claims 38 and 44-46 made in paragraph 16 of the Office Action mailed 11/03/04 under 35 U.S.C. § 112, first paragraph, as containing new subject matter, is withdrawn in light of Applicants' amendments to the claims. A modified rejection is set forth below.

9) The rejection of claims 38 and 44-46 made in paragraph 17 of the Office Action mailed 11/03/04 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendments to the claims.

10) The rejection of claims 38 and 44-46 made in paragraph 19 of the Office Action mailed 11/03/04 under 35 U.S.C. § 102(e)(2) as being anticipated by Cover *et al.* (US 6,054,132, filed 02/26/1992 - already of record) (Cover *et al.*, '132) as evidenced by Harlow *et al.* (*In*: *Antibodies*: *A Laboratory Manual.* Cold Spring Harbor Laboratory, Chapter 5, p. 76, 1988), is withdrawn in light of the new ground of rejection made below.

11) The rejection of claims 38 and 44-46 made in paragraph 20 of the Office Action mailed 11/03/04 under 35 U.S.C. § 102(e)(2) as being anticipated by Cover *et al.* (*J. Biol. Chem.* 267: 10570-10575, 25 May 1992 - already of record) (Cover *et al.*, 1992) as evidenced by Harlow *et al.* (*In*: *Antibodies*: *A Laboratory Manual.* Cold Spring Harbor Laboratory, Chapter 5, p. 76, 1988), is withdrawn in light of the new ground of rejection made below.

Response to Applicants' Arguments on New Matter Rejection

12) Applicants contend that the specification at page 5, lines 31-39, teaches that the term cytotoxin or toxin is a general term referring to the protein of *Helicobacter pylori*. Applicants state that this passage clearly teaches that the precursor protein (which has the amino acid sequence of SEQ ID NO: 3) is a protein of 140 kDa and that the proteolytic fragment has cytotoxic activity (by clear implication and generally accepted terminology in the art, the precursor does not have such activity). Applicants submit that lines 1-11 on page 6 describe the processed fragment being recovered from supernates and having cytotoxic activity. Applicants claim that they are the ones who for the first time discovered that the cytotoxin is actually a processed portion of a much larger

precursor protein. Applicants conclude that one of skill in the art would understand that the precursor protein (having the amino acid sequence of SEQ ID NO: 3) would not be cytotoxic until processed, and thus the polypeptide of SEQ ID NO: 3 would not have cytotoxic activity. Applicants further cite the post-filing references of Vinion-Dubiel *et al.* (1999); McClain *et al.*, 2003; Reyrat *et al.*, 1999; and Genisset *et al.* and state that these references prove that the cytotoxin of *H. pylori* may be altered genetically to produce a cytotoxin that has substantially reduced or no cytotoxicity. Applicants state that this was first taught in the Applicants' specification and has now been borne out by these investigators' work. Applicants assert that the specification teaches that a polypeptide that is 'derived from' a particular nucleic acid sequence is one that has an amino acid sequence encoded by the nucleic acid, is a portion of the encoded sequence, **or** is immunologically identifiable with a polypeptide encoded in the sequence. Applicants state that those of skill in the art would clearly understand that these are not mutually exclusive, despite the Office's overemphasis of the word 'or'. Applicants further state that one of skill in the art would appreciate that not all fragments of the encoded sequence would necessarily be immunologically identifiable with the encoded sequence. Applicants opine that the conjunction 'and' would be inappropriate to express the idea that Applicants convey in the specification. Applicants state that this 'is merely an attribute of the encoded polypeptides and certain polypeptide fragments would be immunologically identifiable with the encoded sequence'. Applicants contend that all the immunologically identifiable fragments would be at least 3-5, 8-10, or 11-15 amino acids in length and pose the question: 'How could it be otherwise'? Applicants state that it is puzzling that the Office is not persuaded that the original claim 8 supports the subject matter that the polypeptides have the two functional aspects of being immunologically identifiable with antibodies that react specifically with the full-length protein (SEQ ID NO: 3) and which have no or reduced cytotoxicity. Applicants contend that the original claim 8 adds the limitation that the polypeptides have no or reduced cytotoxicity, or substantially reduced cytotoxicity, and therefore the claims, as originally filed, clearly contemplated the precursor and fragments of the polypeptide having no or reduced cytotoxicity. Applicants state that the portions of the amino acid sequence were also said to include those that were immunologically identifiable with the encoded protein.

Applicants' arguments have been carefully considered, but are non-persuasive. The descriptive support for the claim limitations has to come from Applicants' specification, as

originally filed, and not from the post-filing references of Vinion-Dubiel *et al.* (1999); McClain *et al.*, 2003; Reyrat *et al.*, 1999; and Genisset *et al.* Contrary to Applicants' assertion, the specification at page 5, lines 31-39, does not teach that the term cytotoxin or toxin is a 'general term' referring to the protein of *Helicobacter pylori.* This part of the specification does not associate a precursor cytotoxin having the amino acid sequence from Figure 2 (i.e., SEQ ID NO: 3) to 'reduced cytotoxic activity' or 'no cytotoxic activity'. Contrary to Applicants' assertion, lines 1-11 on page 6 do not describe any fragment 'being recovered from supernates and having cytotoxic activity'. Contrary to Applicants' contention, lines 1-11 on page 6 of the specification describe a 87 kDa polypeptide 'previously described' by Cover *et al., J. Biol. Chem.* 267: 10570-75, 1992. Furthermore, Applicants' express argument that the precursor protein having the amino acid sequence of SEQ ID NO: 3 would not be cytotoxic until processed and thus the polypeptide of SEQ ID NO: 3 would not have cytotoxic activity, provides the *prima facie* evidence for lack of support for a polypeptide of SEQ ID NO: 3 or a fragment thereof that is immunologically identifiable as recited *and* that exhibits 'reduced cytotoxic activity compared with *Helicobacter pylori* cytotoxin purified from cell cultures'. How can a polypeptide of SEQ ID NO: 3 which is asserted to have no cytotoxic activity exhibit 'reduced cytotoxic activity compared with *Helicobacter pylori* cytotoxin purified from cell cultures'?

The specification at lines 21-30 of page 14 describes a polypeptide which consists of at least 3-5 amino acids, and more preferably at least 8-10 amino acids, and even more preferably at least 11-15 amino acids, **or** a polypeptide which is immunologically identifiable with a 'polypeptide encoded in the sequence'. The limitation 'and' appearing between parts (i) and (ii) of the instant claims requires that the claimed polypeptide or fragment thereof have the function recited in part (i) **and** the function recited in part (ii) of the claim. The recitation 'or' in the specification is given its normal meaning. Applicants appear to insist that the Office should interpret the limitation 'or' as being equivalent to the term 'and'. However, doing so would be improper under the procedure permitted within MPEP.

The original claim 8, and claims 3, 2 and 1 from which it depends, are reproduced below:

8. The recombinant protein according to claim 2 or 3 wherein the recombinant protein exhibits substantially no toxicity, or substantially reduced toxicity.
3. The recombinant protein according to claim 2 wherein the cytotoxin, precursor, derivative or fragment thereof has the amino acid sequence of Figure 2, or a portion thereof.
2. The recombinant protein according to claim 1 wherein the protein is a Helicobacter pylori cytotoxin or a

precursor, derivative or fragment thereof.

1. A recombinant Helicobacter pylori protein, or a derivative or fragment thereof.

Thus, the recombinant *Helicobacter pylori* cytotoxin protein or a precursor, derivative or fragment thereof having 'the amino acid sequence of Figure 2', or a portion thereof claimed in these original claims, particularly claim 8, is not associated with immunological identifiability by antibodies that react specifically with the polypeptide having the amino acid sequence of SEQ ID NO: 3. These original claims, including claim 8, are not drawn to a purified recombinant cytotoxin which exhibits no cytotoxic activity or reduced cytotoxic activity compared with *Helicobacter pylori* cytotoxin purified from cell cultures and which is immunologically identifiable by antibodies that react specifically with the polypeptide having the amino acid sequence of SEQ ID NO: 3. The 'fragment', 'derivative' and 'portion' thereof that are recited in the above-cited original claims do not have a size or length limit in addition to having no association with immunological identifiability by antibodies that react specifically with the polypeptide having the amino acid sequence of SEQ ID NO: 3. Clearly, the product claimed in these original claims is not associated with the two functions that are recited in the instant claims. Furthermore, Figure 2 recited in claim 3 depicts one single amino acid sequence that is 1296 amino acid residues-long. This single polypeptide sequence from Figure 2 can either be the amino acid sequence of the precursor cytotoxin or the cytotoxin. The single polypeptide of SEQ ID NO: 3 from Figure 2 cannot represent both the cytotoxic cytotoxin and the non-cytotoxic or less toxic precursor cytotoxin. The description of the drawings at lines 28 and 29 of page 4 of the specification describes that Figure 2 represents SEQ ID NO: 3, 'the amino acid sequence for the cytotoxin (CT) protein'. One of skill in the art would understand the described 'cytotoxin (CT) protein' to be cytotoxic. The Figure 2 description does not identify SEQ ID NO: 3 to be the cytotoxin precursor. However, on page 5 of their amendment filed 04/04/05, Applicants assert that the amino acid sequence of SEQ ID NO: 3 represents the 140 kDa full length precursor cytotoxin, which requires proteolytic processing to generate the 100 kDa, or 87 kDa cytotoxic protein of 100 kDa. The single amino acid sequence from Figure 2 does not and cannot represent a polypeptide having a range of molecular weight, no or reduced cytotoxic activity, and concurrently having the function of immunological identifiability by antibodies that react specifically with the polypeptide having the amino acid sequence of SEQ ID NO: 3. For the reasons delineated above, the rejection set forth below is proper.

Rejection(s) under 35 U.S.C. § 112, First Paragraph (New Matter)

13) Claims 38 and 44-46 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claims 38 and 44-46 now include the new limitations: 'purified' polypeptide ..... exhibits 'no cytotoxic activity or reduced cytotoxic activity compared with *Helicobacter pylori* cytotoxin purified from cell cultures'. Accordingly, the claims are now drawn to an immunogenic composition comprising an immunologically effective amount of a purified polypeptide or purified recombinantly produced polypeptide comprising the amino acid sequence of SEQ ID NO: 3, or a purified recombinant polypeptide fragment of the amino acid sequence of SEQ ID NO: 3, which polypeptide is *required* to have the *two* functional properties: (a) immunological identifiability by antibodies that react specifically with the polypeptide having the amino acid sequence of SEQ ID NO: 3 *and*, (b) exhibition of no cytotoxic activity or reduced cytotoxic activity compared with *Helicobacter pylori* cytotoxin purified from cell cultures. However, there is no descriptive support in the specification, as originally filed, for such a purified recombinant polypeptide comprising the amino acid sequence of SEQ ID NO: 3 and concurrently having the two recited functions. Applicants do not point to a specific portion of the specification for descriptive support for the limitation: 'compared with *Helicobacter pylori* cytotoxin purified from cell cultures'. A review of the specification indicates that the new limitations added at the end of the claims are not supported. Therefore, the limitations in the claims are considered to be new matter. A composition as claimed comprising a purified polypeptide having the recited functions **and** the structure is not supported. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P 608.04 to 608.04(c).

Applicants are respectfully requested to remove the new matter from the claim(s), or point to specific pages and line numbers in the specification, as originally filed, where support for such recitations can be found.

Rejection(s) under 35 U.S.C. § 102

14) Claims 38 and 44-46 are rejected under 35 U.S.C § 102(b) as being anticipated Manetti *et al.* (*Infect. Immun.* 65: 4615-4619, November 1997) (Manetti *et al.*, 1997).

Instant claims are not granted priority to the PCT application because of the new matter added to the claims as identified above.

Manetti *et al.* (1997) taught an immunogenic composition comprising a solution of aluminum hydroxide (i.e., pharmaceutically acceptable carrier) and a highly purified VacA cytotoxin of *H. pylori* CCUG17874 that is mildly formaldehyde-inactivated (i.e., toxoided). The composition induced high titer *H. pylori* cytotoxin-specific antibodies (therefore immunogenic) in rabbits (see abstract; right column on pages 4615 and 4617). The formaldehyde-treated VacA exhibited reduced toxicity compared with native *H. pylori* cytotoxin purified from the culture supernatant of *H. pylori* CCUG17874, retained antigenic integrity and reacted with a purified immunoglobulin from a rabbit serum raised against native VacA (see first paragraph under 'Materials and Methods'; Figures 1 and 2; and page 4616). Although Manetti *et al.* (1997) are silent about the SEQ ID number(s) as recited, since the prior art polypeptide is produced by the same CCUG 17874 strain of *H. pylori* as that of Applicants' strain (see sections 'Materials and methods' and 'Results' of the instant specification), the prior art polypeptide is expected to necessarily have the same structure and the amino acid sequence as recited in the instant claims.

The limitation 'recombinant' or 'recombinantly produced' in the instant claims is viewed as a process limitation in product claims. It should be noted that when claims are drawn to a product-by-process, claims are not limited to the manipulations of the recited step(s), but only the structure implied by the steps. MPEP § 2113 states:

> [E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. *In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)* (citations omitted).

A product does not have to be made by the same process in order to be the same product, because a product is a product, no matter how it is claimed. Applicants have not shown that the alleged difference(s) in the isolation process results in a product that is structurally different from the product of the prior art.

Claims 38 and 44-46 are anticipated by Manetti *et al.* (1997).

15) Claims 38 and 44-46 are rejected under 35 U.S.C. § 102(b) as being anticipated by McGuinnes *et al.* (*J. Exp. Med.* 171: 1871-1882, 1990).

It is noted that a portion of the polypeptide is described in the second full paragraph of page 14 of the instant specification include a portion that consists of at least three amino acids.

McGuinnes *et al.* taught a synthesized (therefore purified) tripeptide consisting of the NNT sequence containing a minimum reactive epitope, which retained the ability to be antigenic, i.e., antibody-binding ability (see Figure 4g; bottom of page 1875; and part (c) on page 1878). The peptide is contained in a solution (i.e., pharmaceutically acceptable carrier). See third full paragraph on page 1873. The reference of McGuinnes *et al.* does not attribute any degree of cytotoxicity to the tripeptide. Therefore, the NNT sequence of McGuinnes *et al.* serves as a fragment of the instantly recited polypeptide being located at positions 336-338 of the instantly recited SEQ ID NO: 3. That the peptide NNT present in the prior art solution (i.e., composition) is immunologically identifiable by an antibody that reacts specifically with *H. pylori* cytotoxin and exhibits no or reduced toxicity compared with *H. pylori* cytotoxin purified from cell cultures is inherent from the teachings of McGuinnes *et al.* since the NNT peptide is structurally identical with a three amino acid-long fragment of the instantly recited SEQ ID NO: 3. Since the prior art peptide is structurally identical to the NNT fragment of the instant SEQ ID NO: 3, it is expected have the same functions as recited in parts (i) and (ii) of the instant claims. Therefore, the prior art composition comprising an immunoreactive epitope-containing NNT peptide sequence anticipates the instantly claimed composition.

The limitation 'recombinant' or 'recombinantly produced' in the instant claims is viewed as a process limitation in product claims. It should be noted that when claims are drawn to a product-by-process, claims are not limited to the manipulations of the recited step(s), but only the structure implied by the steps. MPEP § 2113 states:

> [E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. *In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)* (citations omitted).

A product does not have to be made by the same process in order to be the same product, because a product is a product, no matter how it is claimed. Applicants have not shown that the alleged difference(s) in the isolation process results in a product that is structurally different from the product of the prior art.

Claims 38 and 44-46 are anticipated by McGuinnes *et al.*

16) Claims 38 and 44-46 are rejected under 35 U.S.C. § 102(b) as being anticipated by Palker *et al.* (*PNAS* 85: 1932-1936, 1988) as evidenced by McGuinnes *et al.* (*J. Exp. Med.* 171: 1871-1882, 1990).

The transitional recitation 'comprising' in the instant claims is open-ended claim language and therefore does not exclude additional, unrecited elements. See MPEP 2111.03 [R-1].

It is noted that the minimum size required in the instant specification for a 'portion' (i.e., fragment) of the polypeptide is described as three amino acids. See the second full paragraph of page 14 of the instant specification. Applicants' contention that all the immunologically identifiable fragments would be at least 3-5, 8-10, or 11-15 amino acids in length has also been noted. See lines 3-6 on page 7 of Applicants' amendment/response filed 04/04/05.

Palker *et al.* taught an antigenic conjugate composition wherein a synthetic peptide containing the sequence Asn-Asn-Thr (NNT), i.e., purified polypeptide fragment of the amino acid sequence of SEQ ID NO: 3, is chemically conjugated to a protein carrier, such as, BSA or tetanus toxoid. The conjugate induced antibodies in goats on immunization with an adjuvant. See abstract; Materials and Methods; Results; Figure 1 and Table 1. The NNT sequence of Palker *et al.* serves as a fragment located at positions 336-338 of the instantly recited SEQ ID NO: 3. The reference of Palker *et al.* does not attribute any degree of cytotoxicity to the tripeptide. That the peptide NNT present in the prior art conjugate composition is immunologically identifiable by an antibody that reacts specifically with *H. pylori* cytotoxin and exhibits no or reduced toxicity compared with *H. pylori* cytotoxin purified from cell cultures is inherent from the teachings of Palker *et al.* since the NNT peptide is structurally identical with a three amino acid-long fragment of the instantly recited SEQ ID NO: 3. Since the prior art peptide is structurally identical to the NNT fragment of the instant SEQ ID NO: 3, it is expected have the same functions as recited in parts (i) and (ii) of the instant claims. Therefore, the prior art composition comprising an immunogenic NNT-containing peptide sequence anticipates the instantly claimed composition. That the NNT peptide sequence in

the prior art immunogenic composition contains an epitope is inherent from the teachings of Palker *et al.* in light of what is well known in the art. For instance, McGuinness *et al.* taught that the NNT peptide sequence contains a minimum reactive epitope (see Figure 4g; bottom of page 1875; and part (c) on page 1878).

Thus, an immunogenic composition comprising a purified polypeptide fragment of the instantly recited SEQ ID NO: 3 existed in the prior art well before the effective filing date of the instant invention. The teachings of Palker *et al.* anticipate the instant claims. McGuinness *et al.* is **not** used as a secondary reference in combination with Palker *et al.*, but rather is used to show that every element of the claimed subject matter is disclosed by Palker *et al.* with the unrecited limitation(s) being inherent in view of what is known in the art as explained above. See *In re Samour* 197 USPQ 1 (CCPA 1978).

The limitation 'recombinant' or 'recombinantly produced' in the instant claims is viewed as a process limitation in product claims. It should be noted that when claims are drawn to a product-by-process, claims are not limited to the manipulations of the recited step(s), but only the structure implied by the steps. MPEP § 2113 states:

> [E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. *In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)* (citations omitted).

A product does not have to be made by the same process in order to be the same product, because a product is a product, no matter how it is claimed. Applicants have not shown that the alleged difference(s) in the isolation process results in a product that is structurally different from the product of the prior art.

17) Claims 38 and 44-46 are rejected under 35 U.S.C. § 102(b) as being anticipated by Cover *et al.* (*J. Biol. Chem.* 267: 10570-10575, 25 May 1992 – already of record) (Cover *et al.*, 1992).

Instant claims are not afforded the priority benefit to PCT application(s), or to the foreign priority application, FI 92A000052 filed 03/02/92, since these applications lack descriptive support for the limitations: 'compared with *Helicobacter pylori* cytotoxin purified from cell cultures', and/or for a purified polypeptide or recombinantly produced polypeptide comprising the amino acid sequence of SEQ ID NO: 3, having the two *required* functional properties of: (a) immunological

identifiability by antibodies that react specifically with the polypeptide having the amino acid sequence of SEQ ID NO: 3 *and*, (b) no cytotoxic activity or reduced cytotoxic activity compared with *Helicobacter pylori* cytotoxin purified from cell cultures.

It is noted that the transitional recitation 'comprising' represents open-ended claim language and therefore does not exclude additional, unrecited elements. See MPEP 2111.03 [R-1].

Cover *et al.* (1992) taught an immunogen comprising an isolated denatured *Helicobacter pylori* protein having a molecular weight of 87,000 which elicited antibodies to the protein on immunization of rabbits (see first full paragraph in right column on page 10571; and right column on page 10574). The protein comprised a 23 amino acid-long amino terminal portion having the sequence, AFFTTVIIPAIVGGIATGTAVGT, which amino terminal sequence has 100% sequence identity with a 23 amino acid-long contiguous polypeptide fragment that stretches between positions 34-56 of the instantly recited SEQ ID NO: 3 (see the very first sequence depicted at the top portion of Cover's Table III). The 'denatured' immunogenic protein of the prior art comprising the N-terminal sequence AFFTTVIIPAIVGGIATGTAVGT is expected to have the inherent ability to be immunologically identifiable by antibodies that react specifically with the polypeptide having the amino acid sequence of SEQ ID NO: 3 and is expected to have reduced cytotoxic activity compared with *Helicobacter pylori* cytotoxin purified from cell cultures.

The term 'recombinant' or 'recombinantly produced' in the instant claims represents a process limitation in product claims. The prior art polypeptide anticipates the instantly claimed polypeptide, irrespective of how it is obtained. When claims are drawn to a product-by-process, claims are not limited to the manipulations of the recited step(s), but only the structure implied by the steps. MPEP § 2113 states:

> [E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. *In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)* (citations omitted).

A product does not have to be made by the same process in order to be the same product, because a product is a product, no matter how it is claimed. Applicants have not shown that the alleged difference(s) in the process results in a product that is structurally different from the product of the prior art. In the instant case, Applicants have not shown that the underlying structure of the prior art polypeptide comprising the above-identified 23 amino acid-long N-terminal fragment differs from

the instantly recited polypeptide of the amino acid sequence SEQ ID NO: 3 comprising the same structurally identical N-terminal fragment.

Claims 38 and 44-46 are anticipated by Cover *et al.* (1992).

Remarks

18) Claims 38 and 44-46 stand rejected.

The amino acid sequence of SEQ ID NO: 3 is free of prior art currently of record.

19) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The central Fax number for submission of amendments, responses and papers is (703) 872-9306.

20) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.Mov. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

21) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system. A message may be left on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (571) 272-0864.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

June, 2005

S. DEVI, PH.D.
PRIMARY EXAMINER